administration to any tissue or organ having an epithelial membrane. The delivery-enhancing agents include detergents, alcohols, surfactants and other molecules.--

IN THE CLAIMS:

Please cancel claims 21, 22, 35, 36, 40, 54 and 55 without prejudice or disclaimer.

REMARKS

Claims 41-53 are pending in this application and are presented for examination. Claims 21, 22, 35, 36, 40, 54 and 55 have been canceled without prejudice. Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

Reconsideration of the application is respectfully requested in view of the above amendments to the claims and the following remarks. For the Examiner's convenience and reference, Applicants' remarks are presented in the order in which the corresponding issues were raised in the Office Action.

In view of the cancellation of claim 22, the misspelling of mucoadhesive is now a moot point.

Applicants acknowledge the withdrawal of the rejections under 35 U.S.C. § 102(b) and 103(a). In an earnest effort to expedite prosecution of the application, Applicants have canceled claims 21, 22, 35, 35, 40, 54 and 55 drawn to methods of using the current compounds.

I. FIRST REJECTION UNDER 35 U.S.C. § 112, first paragraph

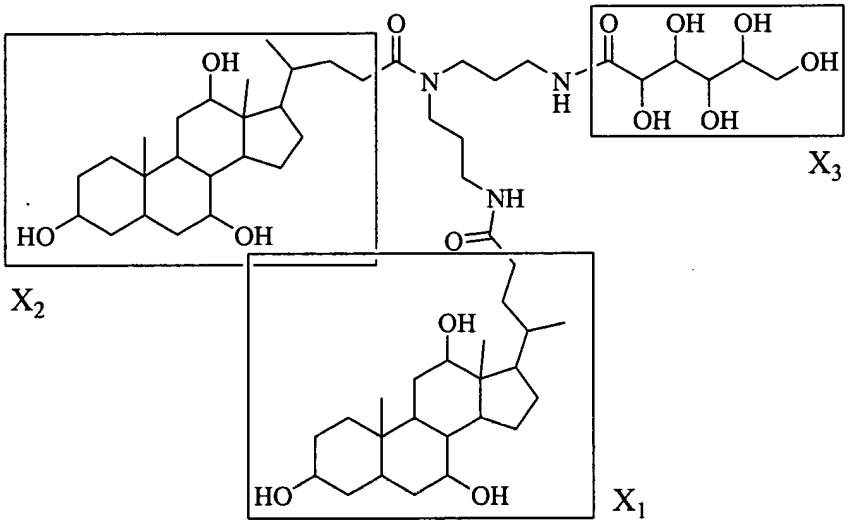
Claims 21, 22, 35, 36 and 40-55 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in

such a way as to reasonably convey to one skilled in the relevant art that the inventors, had possession of the claimed invention. In response, Applicants respectfully traverse the rejection.

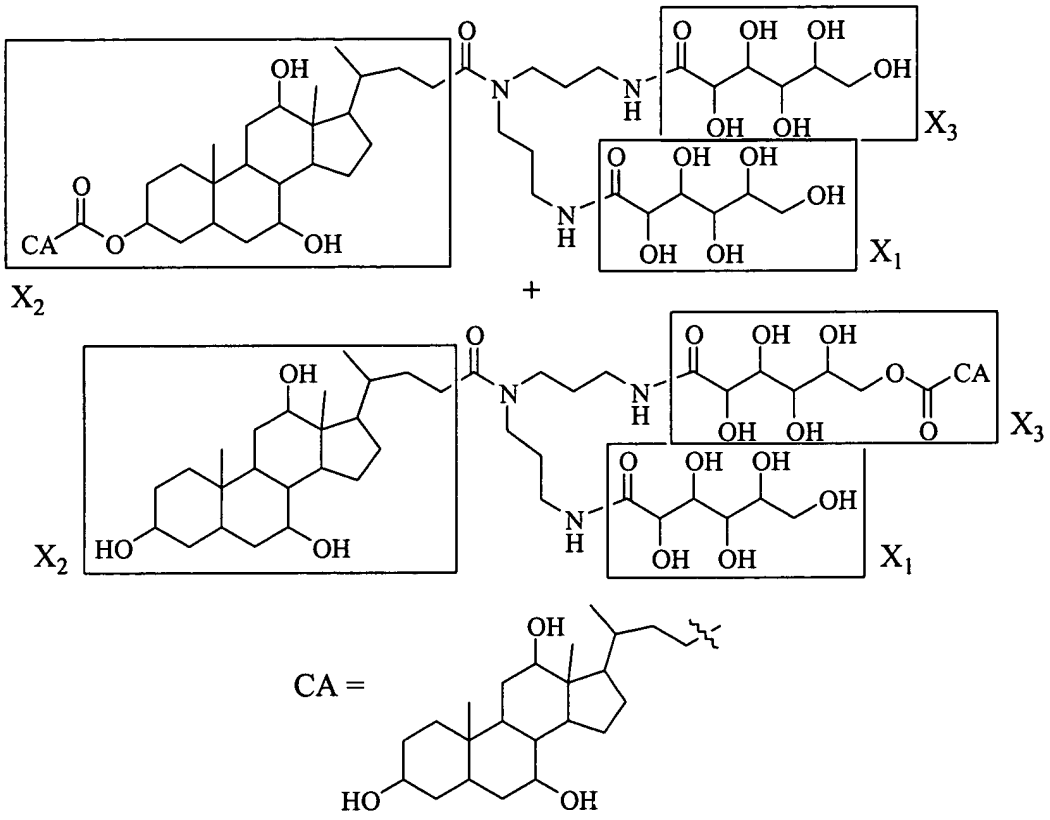
A. The Structure of Impurity II is Disclosed and Claimed.

As the Examiner states in the present Office Action, the structures of the impurities have been determined in Application No. 09/112,074 (now US Patent No. 6,392,069). Applicants respectfully point out that it appears that the Examiner has incorrectly assigned Impurities II and III. At column 29, line 14-16, US Patent No. 6,392,069 states that "[S]pectra of Impurity 2 are shown in FIG. 23, and those of Impurity 3 are shown in FIG. 24." The structures of Impurities 2 and 3 are reproduced below with X_1, X_2 and X_3 from Formula I of the instant application labeled for the Examiner's convenience.

Impurity 2 - Impurity II

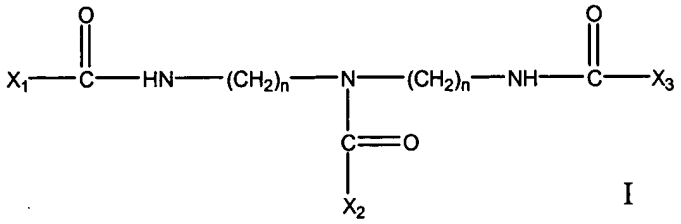


Impurity 3 - Impurity III



There are two structures for Impurity III because the second cholic acid group can be bound to the primary structure by reacting with one of several primary and secondary alcohols, yielding the two structures shown above.

Applicants agree that BigCHAP and Impurity I do not correlate to Formula I, as set forth below.



I

Applicants further agree with the Examiner that, for Impurity III, since X_1 is a saccharide group, this does not correlate to Formula I. However, Formula I does read on Impurity II, as demonstrated below and in the specification.

B. Written Description of Impurity II Meets the Requirements of 35 U.S.C. § 112, 1st paragraph

The Examiner alleges that the specification lacks written description for the impurities in Big CHAP. The Examiner states:

> In Impurity III, the specification does not describe the impurity as having two cholic acid groups (and not deoxycholic acid groups) as X1 and X2 or X3. The specification does not describe X2 or X3 as a pentose monosaccharide. Therefore, the structure of Impurity III is not readily apparent from the specification as originally filed because the specific combination of elements in X1, X2 or X3 could not have been guessed.

As discussed above, Impurity II was apparently mistaken as Impurity III by the Examiner. As such, Applicants respectfully traverse the rejection.

Applicants point out to the Examiner that the specification on page 3, line 15- 21 states:

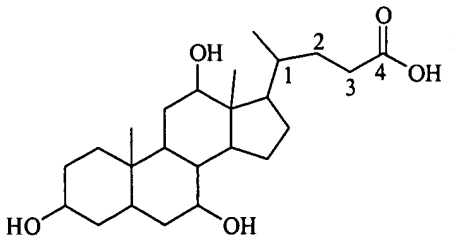
> X_1 is a **cholic acid group** or **deoxycholic acid group**; and X_2 and X_3 are each independently selected from the group consisting of a **cholic acid group, a deoxycholic acid group, and a saccharide group**, wherein the saccharide group is selected from the group consisting of **pentose monosaccharide groups**, hexose monosaccharide groups, pentose-pentose disaccharide groups, hexose-hexose disaccharide groups, pentose-hexose disaccharide groups, and hexose-pentose disaccharide groups; and wherein at least one of X_2 and X_3 is a saccharide group. (Emphasis added)

This description of Formula I clearly states that the Impurity, such as Impurity II, can have two cholic acid groups (and not deoxycholic acid groups) as X_1 and X_2 or X_3. Additionally, the specification unambiguously states that X_3 can be a pentose monosaccharide. Therefore, Impurity II is fully described. Furthermore, Example 12 in the instant application exhaustively illustrates the synthetic procedure for Impurity II. As a result, Applicants respectfully request that the rejection be withdrawn.

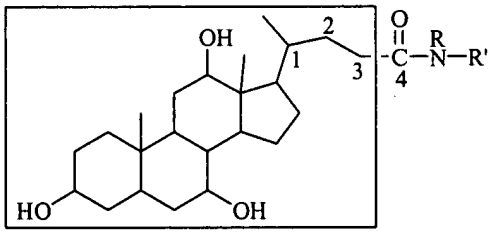
C. Structure of "Cholic Acid Group"

The Examiner further alleges that the specification does not disclose Impurity II as having "a cholic acid group" since "[c]holic acid having a deletion of the terminal CO_2H is not a 'cholic acid group' as claimed because it is no longer cholic acid." In response, Applicants respectfully traverse the rejection.

To a person skilled in the art, it is abundantly clear that the phrase "cholic acid group" means that it is not a cholic acid any longer, but rather a derivative of cholic acid. The Examiner describes the cholic acid group as "cholic acid having a deletion of the terminal CO_2H." Applicants respectfully point out that a "cholic acid group" has not had the terminal CO_2H deleted, but rather substituted. In the instant case, this substitution has resulted in an amide bond. The Examiner's attention is respectfully directed to page 11 of this response and the comments on pages 9-10 wherein the synthetic procedure and bond connectivity of Impurity II is described. In fact, comparing the two structures below of "cholic acid" and "a cholic acid group", the Examiner can plainly see that the only difference is the atoms used in the connectivity of the cholic acid group to Formula I.



Cholic acid



Cholic acid group

As set forth in MPEP § 2111.02:

> Applicant may be his or her own lexicographer as long as the meaning assigned to the term is not repugnant to the term's well known usage. In re Hill, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). Any special meaning assigned to a term "must be sufficiently clear in the specification that any departure from common usage would be so understood by a person of experience in the field of the invention." Multiform Desiccants Inc. v. Medzam Ltd., 133 F.3d 1473, 1477, 45 USPQ2d 1429, 1432 (Fed. Cir. 1998).

Applicants are allowed to be their own lexicographer and define a term in a manner that would be sufficiently clear in the specification and understood by a person of experience in the field. In the instant case, Applicants have chosen to define the term "cholic acid group" as cholic acid without the terminal CO_2H. This is clearly well within Applicants' rights, and would be understood by a person skilled in the art. For example, when Applicants set forth "cholic acid group" in the specification on page 9, line 8, this would be read in conjunction with Example 12. Example 12 clearly states that cholic acid is reacted with isobutylchloroformate in the presence of triethylamine, followed by reaction with 3-aminopropyl-3'-N-gluconamidopropyl-amine to afford to desired product, Impurity II. Clearly this would be understood by a person skilled in the art.

Moreover, after reviewing several patent documents (such as U.S. Patent Nos. 5,856,202; 4,892,816; 4,458,015) wherein "cholic acid group" is used, in no instance does it state that "cholic acid" is the same as "a cholic acid group". Thus, the Examiner's insistence that "cholic acid group" means "cholic acid" is contrary to the clear meaning of cholic acid group in this application and the patent literature. As such, Applicants respectfully request that the Examiner withdraw the rejection.

D. Teaching of Saccharide Groups and Deoxycholic Acid

Additionally, the Examiner alleges that:

> [T]he specification does not teach any compounds having a deoxycholic acid group, a hexose monosaccharide group, a pentose-pentose disaccharide group, a hexose-hexose disaccharide group, a pentose-hexose disaccharide group, or a hexose-pentose disaccharide group.

Applicants respectfully point out, on page 3, line 15-21 of the specification, the following is set forth:

> X_1 is a cholic acid group or **deoxycholic acid group**; and X_2 and X_3 are each independently selected from the group consisting of a cholic acid group, a deoxycholic acid group, and a saccharide group, wherein the saccharide group is selected from the group consisting of pentose monosaccharide groups, **hexose monosaccharide groups, pentose-pentose disaccharide groups, hexose-hexose disaccharide groups, pentose-hexose disaccharide groups, and hexose-**

> **pentose disaccharide groups**; and wherein at least one of X_2 and X_3 is a saccharide group. (Emphasis added)

This description of Formula I clearly teaches compounds that have a deoxycholic acid group, as well as a hexose monosaccharide group, a pentose-pentose disaccharide group, a hexose-hexose disaccharide group, a pentose-hexose disaccharide group, or a hexose-pentose disaccharide group. In addition, Example 12 thoroughly teaches how compounds having these functional groups are utilized to prepare the desired structure. As a result, Applicants respectfully request that the rejection be withdrawn.

E. Written Description for the Genus Claimed Meets the Requirements of 35 U.S.C. § 112, 1st paragraph

The Examiner alleges that:

> [T]he structure of Impurity II and III is not adequate written [description] for all compounds having Formula I or II as claimed which encompasses numerous combinations of X1, X2 and X3. These structures are significantly different and may have different functions than Impurity II or III. Therefore, Impurities II and III are not adequate to describe the genus claimed.

Applicants assert that even a single species is sufficient to claim a genus as a whole. MPEP § 2163 sets forth:

> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. **On the other hand, there may be situations where one species adequately supports a genus**. (Emphasis added)

The instant invention represents a case where even the disclosure of a single species adequately supports a genus. For example, the core of Formula I varies only in the number of carbons linking the nitrogen atoms, a superficial modification. In addition, there are only two choices for substituents for X_2 and X_3: a cholic or deoxycholic acid group; or a simple mono- or disaccharide. The only difference between the cholic and deoxycholic acid group is the absence of a -OH in the latter, something a skilled artisan would recognize as a minor change. In addition, a skilled artisan would also recognize that the change in saccharide group would be an

easy modification given the detailed guidance in the specification. Since the cholic acid and deoxycholic acid are attached to the core in the same manner, and all the saccharide groups are attached to the core in a similar manner, the synthesis of Impurity II in Example 12, for instance, is sufficient description for the preparation of all possible species within the genus. This is the situation where a single species adequately supports a genus. Finally, Applicants would like to remind the Examiner that compounds of Formula II have been canceled. Therefore, Applicants urge the Examiner to withdraw the rejection.

F. Three Carbons Between the Carbonyl Carbon and the Pentose Ring Explained

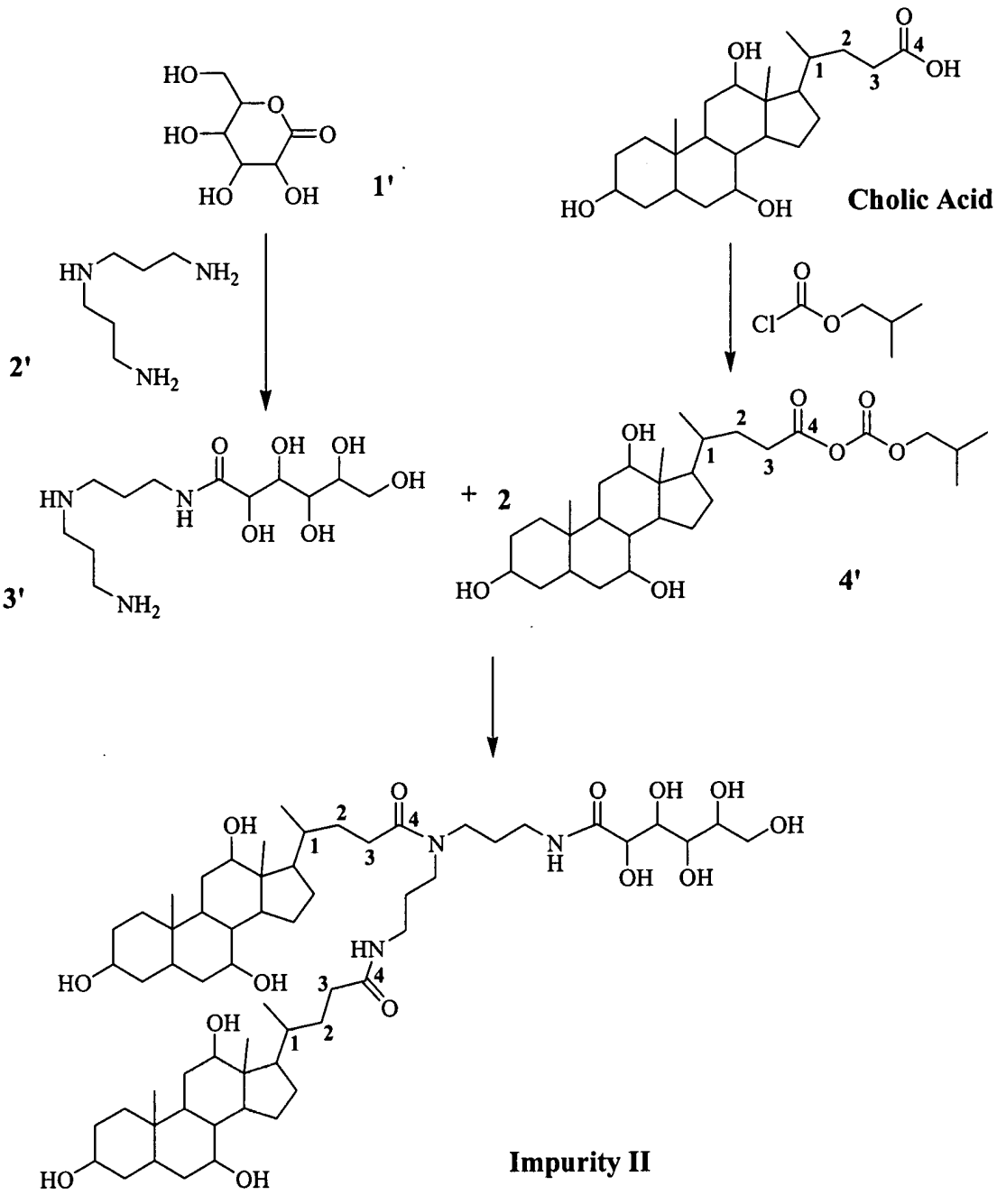
In the previous Office Action dated 7/27/01, and echoed in the most recent Office Action, the Examiner states that:

> In application 09/112,074, the impurities (Fig. III-V) have three carbons between the carboxyl group and the pentose ring of the cholic acid instead of four as in cholic or deoxycholic acid (i.e. the impurities require Xl, X2 or X3 is cholic or deoxycholic acid with a deletion of the terminal O_2H). Addition of the cholic or deoxycholic acid as claimed (with the terminal O_2H) would result in four carbons between the carboxyl group and the pentose ring of the cholic or deoxycholic acid which is not the structure of the impurities disclosed in 09/112,074.

Applicants respectfully suggest that the Examiner may have confused the source of the carbonyl carbon in Impurity II. As Applicants understand it, the Examiner believes that the carbonyl carbon linking the cholic acid group to the rest of the structure does not originate with the starting cholic acid. And thus, in order for Applicants to attach cholic acid to the remainder of the structure, the O_2H has to be removed from the CO_2H, resulting in 4 carbons from the pentose ring to the carbonyl carbon of the core of Formula I. Applicants respectfully disagree with this interpretation.

Applicants point out that the carbonyl carbon linking the cholic acid group to the remainder of the structure originates with the cholic acid starting material. As shown in the synthetic scheme below, the cholic acid starting material has 3 carbons directly linking the pentose ring and the carbonyl carbon. By following carbons 1-4 of the cholic acid through the

synthesis, Applicants show that the carbonyl carbon linking the cholic acid group to the remainder of the structure originates from the cholic acid starting material. Therefore, excluding the branched methyl group, there are *always only* 3 carbons between the pentose ring and the carbonyl carbon linking the cholic acid group to the remainder of the structure. There is no deletion, only a substitution. The -OH of the C(O)OH on the terminus of the cholic acid is substituted with an -NRR' (where R and R' are the remainder of the structure) as shown below.

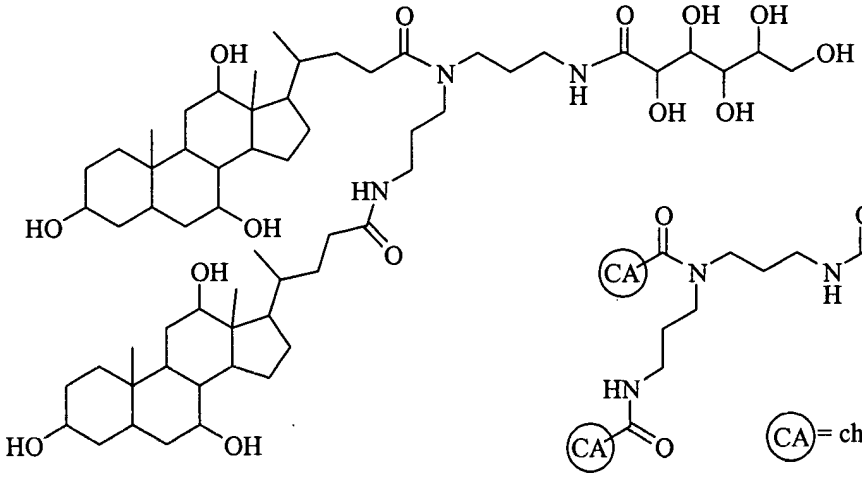


Clearly, a skilled person would be appraised of how to make and use Impurity II with the clear guidance from the present specification. In light of these arguments, Applicants respectfully request the rejection be withdrawn.

G. Disclosure of Synthetic Scheme for Impurity II

As shown above, glucono-δ-lactone (1') is added to iminobispropylamine (2') to afford 3-aminopropyl-3'-N-gluconamidopropyl-amine (3'). In addition, cholic acid is reacted with isobutylchloroformate yielding a mixed anhydride intermediate (4'). Two equivalents of the mixed anhydride intermediate (4') is thereafter reacted with (3') to produce 3'-N-gluconamidopropyl-3''-N-cholamidopropyl-N-cholamide (Impurity II). A person skilled in the art would instantly recognize the above structures by following the synthetic scheme in Example 12, and conclude that the product is Impurity II.

In regards to Example 12 disclosing the synthetic scheme for producing Impurity II, the Examiner states that "Applicants argument is not persuasive because Impurity II (see attached) does not have the structure on pages 6 and 7 of applicants response." Applicants respectfully point out that the Examiner appears to be mistaken in his assignment of Impurity II and III, and that Applicants correctly labeled the structures on pages 6 and 7 of their previous response, shown below for the Examiner's convenience.



Impurity II

Impurity II from previous response

Applicants resubmit arguments that the synthetic scheme in Example 12 unambiguously leads a skilled artisan to Impurity II in the scheme above. The synthetic scheme describing the addition of cholic acid or deoxycholic acid would appraise a skilled artisan of the proper structure for Impurity II. Given this detailed guidance, it is evident that the specification as filed teaches the

attachment of these cholic acid groups in proper context. As such, the Examiner is urged to withdraw the rejection and send this application to issue.

H. Structure of Impurity II is Adequately Described

In regards to the Examiner's allegation that the specification does not describe the structure of Impurity II, Applicants respectfully traverse this allegation. As Impurity II is a species of the claimed genus, Formula I describes the connectivity and functionality of Impurity II. The isolation of Impurity II is also painstakingly disclosed in Example 11 where it states that Big CHAP was first analyzed by Thin Layer Chromatography (TLC) to determine the number of components, and then subjected to column chromatography in order to separate and purify the individual components. Additionally, Example 12 exhaustively describes the synthesis of Impurity II in a manner that would be clear to a person skilled in the art. The synthesis in Example 12 is supported by the presentation of mass spectral data showing the molecular ion of Impurity II. In light of these arguments, Applicants respectfully request that the rejection be withdrawn.

III. SECOND REJECTION UNDER 35 U.S.C. § 112, first paragraph

Claims 21, 22, 35, 36 and 40-55 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. In response, Applicants respectfully traverse the rejection.

Applicants agree with the Examiner that BigCHAP, Impurity I and III do not correlate to the claims.

A. The Structure of Impurity II is Disclosed and Claimed.

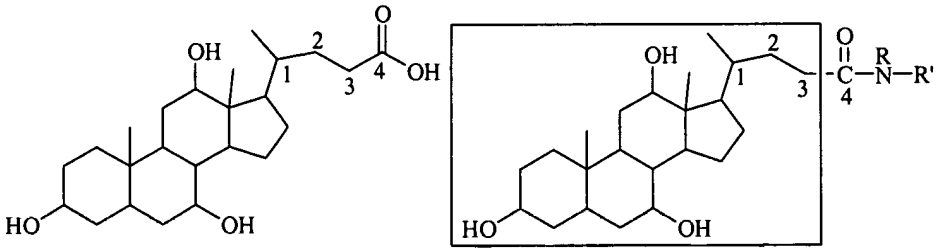
The Examiner alleges that the specification does not teach Impurity II as having two cholic acid groups as X_1 and X_2 or X_3, and X_2 or X_3 as a pentose monosaccharide. As discussed and recited above, the specification unambiguously teaches Impurity II as having two

cholic acid groups and a pentose monosaccharide on page 3, line 15-21 and page 9, line 8-14. As such, Applicants respectfully request that the rejection be withdrawn.

B. The Specification as Filed Meets the Enablement Requirements of 35 U.S.C. § 112, 1st paragraph

The Examiner further alleges that the specification does not disclose Impurity II having a cholic acid group since "[c]holic acid having a deletion of the terminal CO_2H is not a 'cholic acid group' as claimed because it is no longer cholic acid." In response, Applicants respectfully traverse the rejection.

To a person skilled in the art, it is abundantly clear that the phrase "cholic acid group" means that it is not necessarily cholic acid any longer, but rather a derivative of cholic acid. The Examiner describes the cholic acid group as "cholic acid having a deletion of the terminal CO_2H." Again, Applicants respectfully point out that a "cholic acid group" has not had the terminal CO_2H deleted, but rather substituted. In the instant case, this substitution has resulted in an amide bond. By comparing the two structures below of "cholic acid" and "cholic acid group," the Examiner can plainly see that the only difference is the atoms used in the connectivity of the cholic acid group to Formula I.



Cholic acid Cholic acid group

As recited previously, MPEP § 2111.02 states: "Applicant may be his or her own lexicographer..." Applicants are allowed to be their own lexicographer and define a term in a manner that would be sufficiently clear in the specification and understood by a person of experience in the field. In the instant case, the Applicants have chosen to define the term "cholic acid group" as cholic acid without the terminal CO_2H. This is clearly well within Applicants'

rights, and would be understood by a person skilled in the art. As such, Applicants respectfully request that the Examiner withdraw the rejection.

C. Teaching of Saccharide Groups and Deoxycholic Acid

Additionally, the Examiner alleges that:

> [T]he specification does not teach any compounds having a deoxycholic acid group, a hexose monosaccharide group, a pentose-pentose disaccharide group, a hexose-hexose disaccharide group, a pentose-hexose disaccharide group, or a hexose-pentose disaccharide group.

Applicants respectfully point out that page 3, line 15-21 of the specification sets forth:

> X_1 is a cholic acid group or **deoxycholic acid group**; and X_2 and X_3 are each independently selected from the group consisting of a cholic acid group, a deoxycholic acid group, and a saccharide group, wherein the saccharide group is selected from the group consisting of pentose monosaccharide groups, **hexose monosaccharide groups, pentose-pentose disaccharide groups, hexose-hexose disaccharide groups, pentose-hexose disaccharide groups, and hexose-pentose disaccharide groups**; and wherein at least one of X_2 and X_3 is a saccharide group. (emphasis added)

This description of Formula I clearly teaches compounds that have a deoxycholic acid group, as well as a hexose monosaccharide group, a pentose-pentose disaccharide group, a hexose-hexose disaccharide group, a pentose-hexose disaccharide group, or a hexose-pentose disaccharide group. As a result, Applicants respectfully request that the rejection be withdrawn.

D. Written Description for Genus Claimed Meets the Requirements of 35 U.S.C. § 112, 1st paragraph

The Examiner continues by alleging that:

> [T]he structure of Impurity II and III is not adequate written for all compounds having Formula I or II as claimed which encompasses numerous combinations of X1, X2 and X3. These structures are significantly different and may have different functions than Impurity II or III. Therefore, Impurities II and III are not adequate to describe the genus claimed.

Again, Applicants assert that there is sufficient representation of the genus in order to claim the whole. The core of the claimed Formula I varies only in the number of carbons between the nitrogen atoms, a very superficial change. In addition, there are only two choices for substituents X_2 and X_3: a cholic or deoxycholic acid group; and a simple mono- or disaccharide. The only difference between the cholic and deoxycholic acid group is the absence of a -OH in the latter, something a skilled artisan would recognize as a minor change. In addition, the skilled artisan would also recognize that the change in saccharide group as above. Therefore, Applicants urge the Examiner to withdraw the rejection.

E. The Structure and Modification of Impurity II is Taught

The Examiner further alleges that "[t]he specification does not teach the structure of Impurity III and the specification does not teach how to modify Impurity III." Applicants respectfully refer the Examiner to the discussion above regarding the synthetic procedure in Example 12 that describes not only the step-by-step synthesis of Impurity II, but also important analytical data that unambiguously characterizes the product as Impurity II. Therefore, Applicants respectfully request the rejection be withdrawn.

F. The Structure of Impurity II Enables Formula I

In regards to the Examiner's allegation that the specification does not teach the structure of Impurity II, Applicants respectfully traverse the rejection. As Impurity II is a species of the claimed genus, Formula I describes the connectivity and functionality of Impurity II. The isolation of Impurity II is also painstakingly disclosed in Example 11 where it states that Big CHAP was first analyzed by Thin Layer Chromatography (TLC) to determine the number of components, and then subjected to column chromatography in order to separate and purify the individual constituents. Additionally, Example 12 exhaustively describes the synthesis of Impurity II in a manner that would be clear to a person skilled in the art. The synthesis in Example 12 is supported by the presentation of mass spectral data showing the molecular ion. In light of these arguments, the Applicants respectfully request that the rejection be withdrawn.

IV. FIRST REJECTION UNDER 35 U.S.C. § 112, second paragraph

Claims 41-53 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. In response, Applicants respectfully traverse the rejection.

As discussed thoroughly above, Applicants respectfully suggest that the Examiner may have confused the source of the carbonyl carbon in Impurity II, thus leading to confusion about the number of carbons linking the pentose ring to the carbonyl carbon in the claimed compounds. As Applicants understand it, the Examiner believes that the carbonyl carbon linking the cholic acid group to the rest of the structure does not originate with the starting cholic acid. And thus, in order for Applicants to attach cholic acid to the remainder of the structure, the O_2H from the CO_2H of the cholic acid has to be removed, resulting in 4 carbons from the pentose ring to the carbonyl carbon. Applicants respectfully disagree with this interpretation.

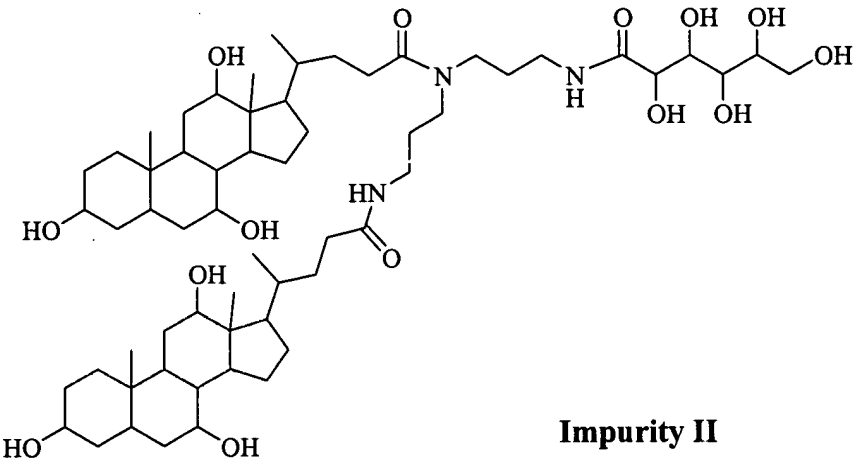
Applicants point out that the carbonyl carbon linking the cholic acid group to the remainder of the structure originates with the cholic acid starting material. As shown in the synthetic scheme previously, the cholic acid starting material has 3 carbons directly linking the pentose ring and the carbonyl carbon. By following carbons 1-4 of the cholic acid through the synthesis, Applicants show that the carbonyl carbon linking the cholic acid group to the remainder of the structure originates from the cholic acid starting material. Therefore, excluding the branched methyl group, there are *always only* 3 carbons linking the pentose ring and the carbonyl carbon linking the cholic acid group to the remainder of the structure. There is no deletion, only a substitution. The -OH of the C(O)OH on the terminus of the cholic acid is substituted with an -NRR' (where R and R' are the remainder of the structure). Therefore, it is clear that Applicants always intended the claim to encompass three carbons between the carbonyl carbon and the pentose ring, and that there is no deletion of the terminal O_2H, simply a substitution. This argument applies to X_1, X_2 and X_3. As such, Applicants respectfully request the rejection be withdrawn.

The Examiner also alleges that "Structure V" disclosed on page 13 of Applicants previous response is not Impurity II. Examiner supports this by stating: "'Structure V' is not disclosed in the specification. Nor are the claims limited to 'Structure V'." In response, Applicants respectfully traverse the rejection.

Applicants clearly and exhaustively disclose not only how to isolate and purify Impurity II, page 29, line 10-22, but also how to synthesize Impurity II, Example 12. In addition, the synthetic procedure provides analytical data in the form of a mass spectral fragmentation pattern, a characteristic unique to Impurity II. As stated previously, a person skilled in the art would understand the synthetic procedure provided in Example 12, and thus would be able to arrive at the product of the synthesis, Impurity II, reproduced below for the Examiner's convenience. In addition, it is not the goal of Applicants to limit the claims to Impurity II, as Impurity II is but a single species within a genus. As set forth in MPEP § 2163:

> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. **On the other hand, there may be situations where one species adequately supports a genus.** (Emphasis added)

This is exactly the situation MPEP 2163 is referring to wherein one species adequately supports a genus. As such, Applicants respectfully request the rejection be withdrawn, and the Examiner send this application to issue.



Impurity II

The Examiner also alleges that it is not readily apparent how the cholic or deoxycholic acid are attached: "[i]t is not readily apparent that the Impurities isolated from BigCHAP would have the terminal O_2H of cholic or deoxycholic acid deleted." Applicants respectfully traverse by pointing out the reasoning made above regarding how the O_2H is not actually deleted, but rather the -OH of the terminal C(O)OH of the cholic or deoxycholic acid is

substituted with an -NRR' group (where R and R' are the remainder of the structure) during the synthetic process, as shown in the previous scheme. Impurity II can either be isolated or synthesized, both procedures yielding the same compound. As such, Applicants respectfully request the rejection be withdrawn.

Examiner's rejection of claim 40 as indefinite as a result of being dependent on a canceled claim is rendered moot in light of the fact that claim 40 has, itself, been canceled.

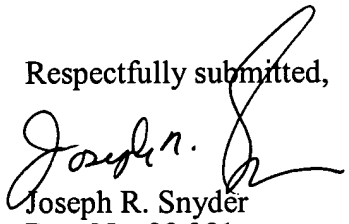
V. OBVIOUSNESS-TYPE DOUBLE PATENTING PROVISIONAL REJECTION

Claims 21, 22, and 44-55 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of copending Application No. 09/112074 (now US Patent No. 6,392,069). In view of the attached Terminal Disclaimer, this rejection is now obviated.

CONCLUSION

In an earnest effort to advance prosecution in this application, Applicants have canceled without prejudice claims drawn to methods of using the subject compounds and compounds of formula II. In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is urged. If the Examiner believes a telephone conference would aid in the prosecution of this case in any way, please call the undersigned at 925-472-5000.

Respectfully submitted,



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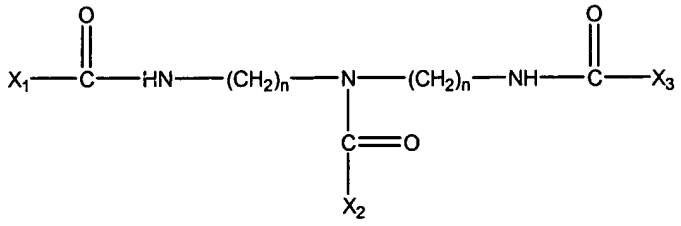
VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

Claims 21, 22, 35, 36, 40, 54 and 55 have been canceled without prejudice. Claims 41-53 are pending.

IN THE ABSTRACT

[A method and pharmaceutical composition for the enhancement of transfer of a therapeutic agent to a cell wherein the therapeutic agent is formulated in a buffer comprising a compound of Formula I:



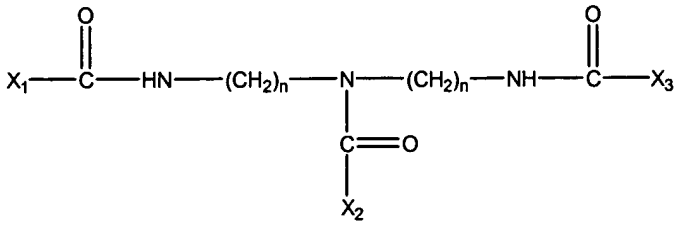
wherein:

n is an integer from 2-8; X1 is a cholic acid group or deoxycholic acid group; and X2 and X3 are each independently selected from the group consisting of a cholic acid group, a deoxycholic acid group, and a saccharide group, wherein the saccharide group is selected from the group consisting of pentose monosaccharide groups, hexose monosaccharide groups, pentose-pentose disaccharide groups, hexose-hexose disaccharide groups, pentose-hexose disaccharide groups, and hexose-pentose disaccharide groups; and wherein at least one of X2 and X3 is a saccharide group.]

The present invention is directed to compositions and methods of treating cancer by gene therapy using a therapeutic gene formulated in a buffer comprising a delivery-enhancing agent. The delivery-enhancing agents of the invention can be used to formulate therapeutic or diagnostic agents, such as proteins, nucleic acids, antisense RNA, small molecules, etc., for administration to any tissue or organ having an epithelial membrane. The delivery-enhancing agents include detergents, alcohols, surfactants and other molecules.

PENDING CLAIMS

41. A compound of Formula I:



wherein:

n is an integer from 2-8;

X_1 is a cholic acid group or deoxycholic acid group; and X_2 and X_3 are each independently selected from the group consisting of a cholic acid group, a deoxycholic acid group, and a saccharide group, wherein the saccharide group is selected from the group consisting of pentose monosaccharide groups, hexose monosaccharide groups, pentose-pentose disaccharide groups, hexose-hexose disaccharide groups, pentose-hexose disaccharide groups, and hexose-pentose disaccharide groups;

and wherein at least one of X_2 and X_3 is a saccharide group.

42. The compound according to claim 41, wherein n is 3.

43. The compound according to claim 41, wherein both X_1 and X_2 are both cholic acid groups and X_3 is a saccharide.

44. The compound according to claim 41, wherein X_1 and X_2 are both deoxycholic acid groups and X_3 is a saccharide group.

45. The compound according to claim 41, wherein the saccharide group is a pentose monosaccharide group.

46. The compound according to claim 41, wherein saccharide group is a hexose monosaccharide group.

47. The compound according to claim 41, wherein the saccharide group is a hexose-hexose disaccharide group.

48. The compound according to claim 41, wherein n is 3, X_1 and X_2 are both cholic acid groups, and X_3 is a hexose monosaccharide group.

49. The compound according to claim 41, wherein n is 3, X_1 and X_3 are both cholic acid groups, and X_2 is a hexose monosaccharide group.

50. The compound according to claim 41, wherein n is 3, X_1 and X_2 are both cholic acid groups, and X_3 is a hexose-hexose disaccharide group.

51. The compound according to claim 41, wherein n is 3, X_1 and X_3 are both cholic acid groups, and X_2 is a hexose-hexose disaccharide group.

52. The compound according to claim 41, wherein n is 3, X_1 and X_2 are both cholic acid groups, and X_3 is a hexose-pentose disaccharide group.

53. The compound according to claim 41, wherein n is 3, X_1 and X_3 are both cholic acid groups, and X_2 is a hexose-pentose disaccharide group.